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# Switching to a dual regimen with the combination of boosted darunavir plus raltegravir in severely experienced patients: a multicentre, retrospective analysis.

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## BACKGROUND

Comorbidities, long-term toxicities, and lack of adherence could be a concern in virologically suppressed, largely experienced, patients receiving complex salvage regimens. Therefore, the emergence of simplified HIV treatment strategies to maintain virological control is a matter of utmost importance.

## OBJECTIVES

There are few data about the safety and efficacy of the combination of a dual regimen with raltegravir (RAL) plus boosted darunavir (b/DRV), as simplification or switching strategy in case of toxicity, especially in patients who had failed successive lines of therapy.

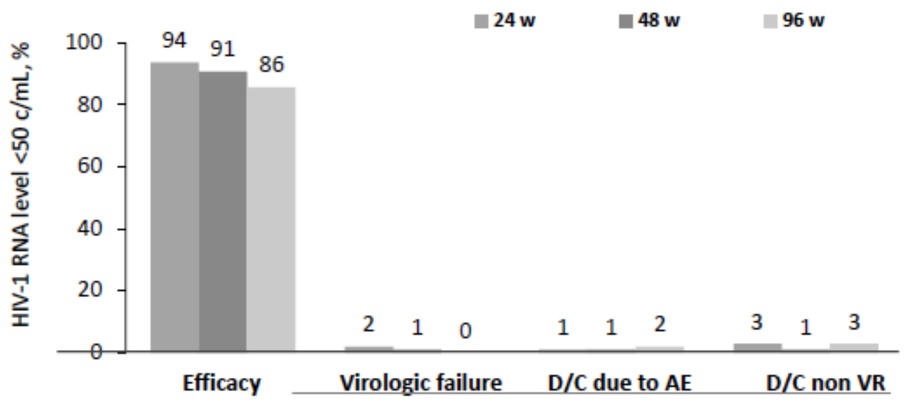
## METHODS

A phase IV, multicentre, retrospective analysis (BIRDi study, **NCT03348449**), including consecutive patients without previous failure to integrase inhibitors, suppressed for more than 48 weeks, was performed in 14 HIV units. The primary end point was the proportion of patients maintaining virologic suppression at 48 and 96 weeks. As secondary endpoints, CD4/CD8 ratio, renal, bone and lipid parameters evolution were assessed.

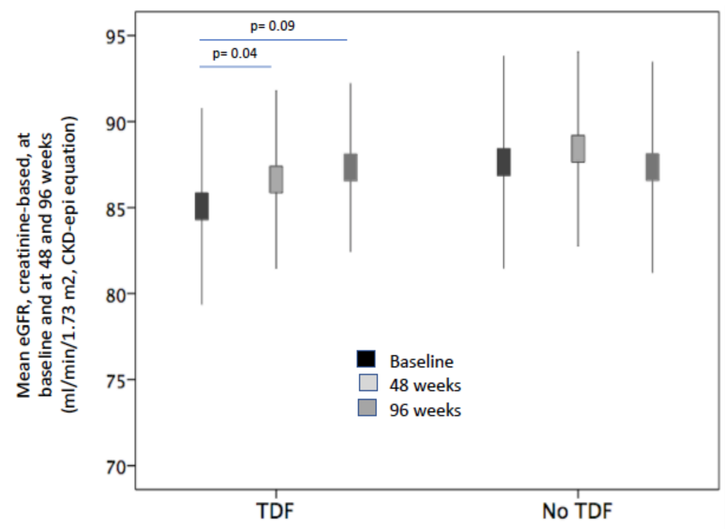
**N= 340 pacientes**
**Baseline characteristics**

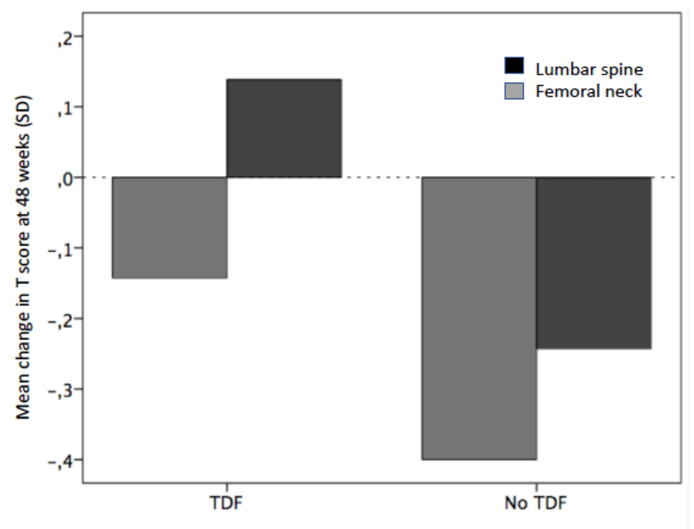
| Variable | Value |
|---|---|
| Mean age, years (range) | 51 (19-82) |
| Sex male, n (%) | 85 (75) |
| Risk factor for HIV infection | |
| Former IDUs, n (%) | 109 (32) |
| MSM, n (%) | 109 (32) |
| HCV coinfection, n (%) | 146 (43) |
| - Fibrosis 4/ Cirrhosis | 24 (16) |
| Duration of HIV infection, yrs | 18.2 (14-22.4) |
| Previous AIDS diagnosis, n (%) | 156 (46) |
| Nadir CD4+T-cell count, cells/ml | 138(53-256) |
| < 200 cells/ml | 214 (63) |
| Prior cART, n (%) | |
| DRV-based | 167 (49) |
| Including a INI | |
| - RAL | 167 (49) |
| TDF-including | 163 (48) |
| Mean number of previous regimens | 9.9 (5-14) |
| Time in previous cART, months | 20.6 (7.7-38) |
| Presence of genotypic resistance to NNRTIs/NRTIs/PI | 184 (54) |
| Mean number of primary mutations against: | |
| NRTIs | 5 (1-7) |
| NRTIS | 3 (1-5) |
| PI | 6 (1-12) |
| GSS to DRV-RAL, mean | 1.78 (1-2) |
| Causes of switch, n (%) | 44 (43) |
| toxicity / intolerance | 146 (43) |
| simplification | 190 (56) |
| non-adherence | 4 (1) |
| Baseline CD4+ cell count, cell/ml | 506 (356-703) |
| Mean CD4/CD8 ratio, median | 0.59 (0.42-0.83) |
| < 0.3 | 48 (14) |
| Mean eGFR (CKD-epi; ml/min/1.73m2) | 85.4 (6-122) |
| MAin comorbidities at inclusion; n (%) | |
| CKD | 54(16) |
| Proteinuria ≥150 mg/gr creatinine (n=34) | 14 (41) |
| Femoral neck/Spine Osteoporosis (n=51) | 5 /11 (10/22) |

## RESULTS

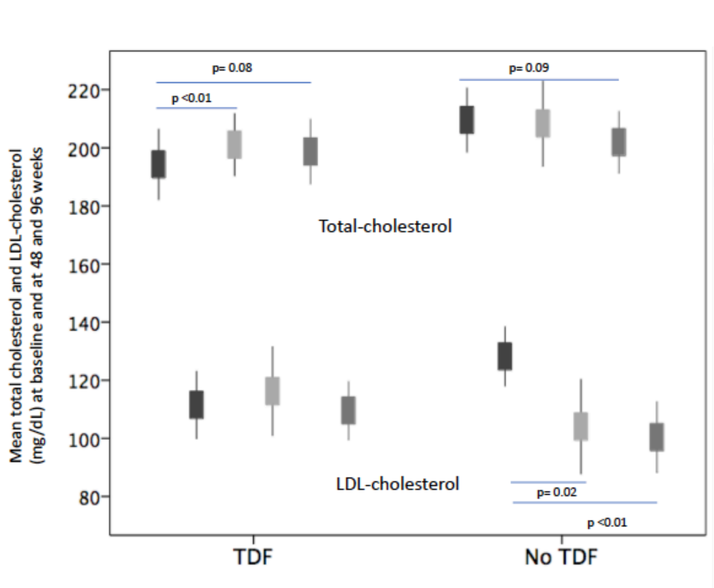


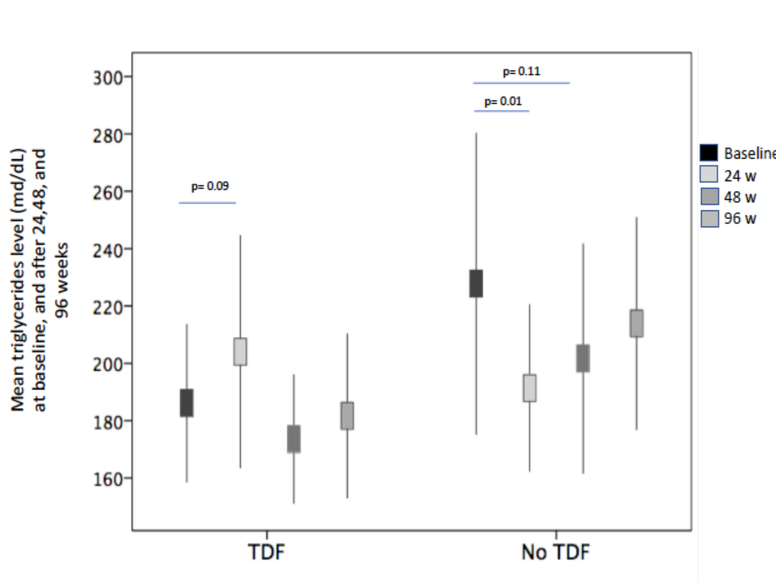

Overall, discontinuation because of virologic failure (VF) throughout the study was rare (0.8%; 95%CI, -0.1%-1.8%). At 48 weeks, 9 patients had detectable HIV RNA level 3%), and efficacy (snapshot analysis) was 91%; (95% CI, 88%-94%): 20 patients (6%) changed therapy because of toxicity (6 patients, 2%; 1 death due to sepsis, 1 increased CK, 1 anxiety, 3 diarrhea), pregnancy (1), drug-drug interactions (8), or were lost to follow up (5). At 96 weeks, efficacy was 86% (95%CI, 83-90%; no additional cases of VF were observed). Median CD4/CD8 ratio increased from 0.59 to 0.66 (p=0.02) and to 0.69, CD4+ count from 560 to 596 cells/mL (p<0.01).




Mean estimated glomerular filtration rate (eGFR) increased from 85.6 to 87.4 and to 88.5 ml/min at 48 and 96 w. This improvement was greater for patients previously receiving TDF (eGFR, +3.6 ml/min, p=0.04; serum phosphate +0.27 mg/dl; p=0.05). DXA scan improved in 33 patients with spine T score from -1.43 to -1.29; p=0.13). Overall, total cholesterol and LDL-c increased for +5% (p=.02) and +9.1% at 48 w, partly corrected at 96 w, an effect due to TDF discontinuation, with improvement in the rest of patients.




## CONCLUSIONS

**A dual treatment with the combination of raltegravir and boosted darunavir is associated with maintenance of virologic suppression, even in severely experienced patients, and with improvements in CD4+ count, CD4/CD8 ratio, and in renal and bone toxicity.**

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